(Bio)Artificial
Organs

(Bio)artificial kidney - new developments

Prof. Dr. Dimitrios Stamatialis

UNIVERSITY OF TWENTE. | TECHMED CENTRE

Potential conflicts of interest declaration

Berliner DialyseSeminar

The content of the following speech is the result of efforts to achieve the maximum degree of impartiality and independence.

As a speaker, I hereby affirm that there are **no conflicts of interest** concerning the content of the following speech that are the result of employment, an advisory function or financial contributions for research projects, lectures or any other activity.

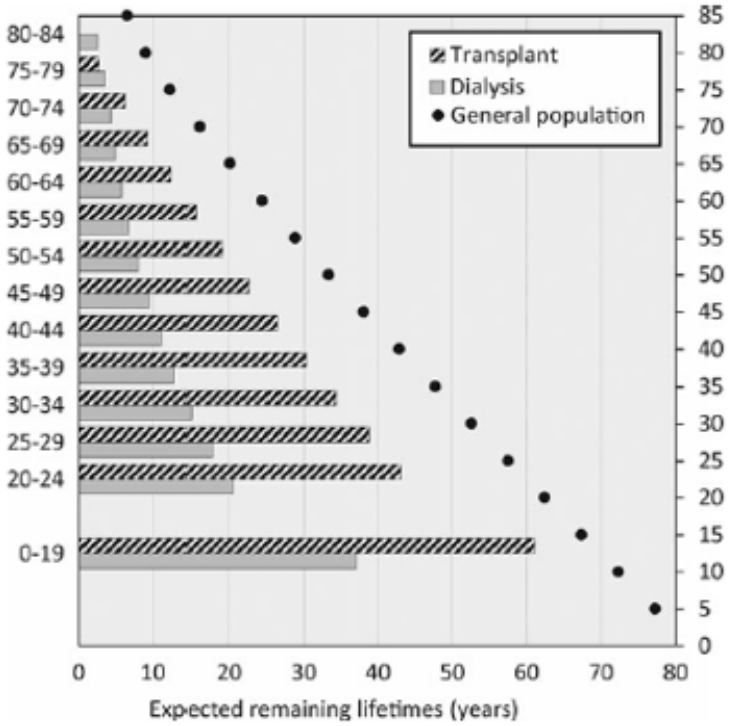
Renal replacement therapy

Dialysis and kidney transplantation

~ 13000 in The Netherlands

Dialysis patients

~ 6500 The Netherlands
~ 350000 Europe
~ 3 million worldwide

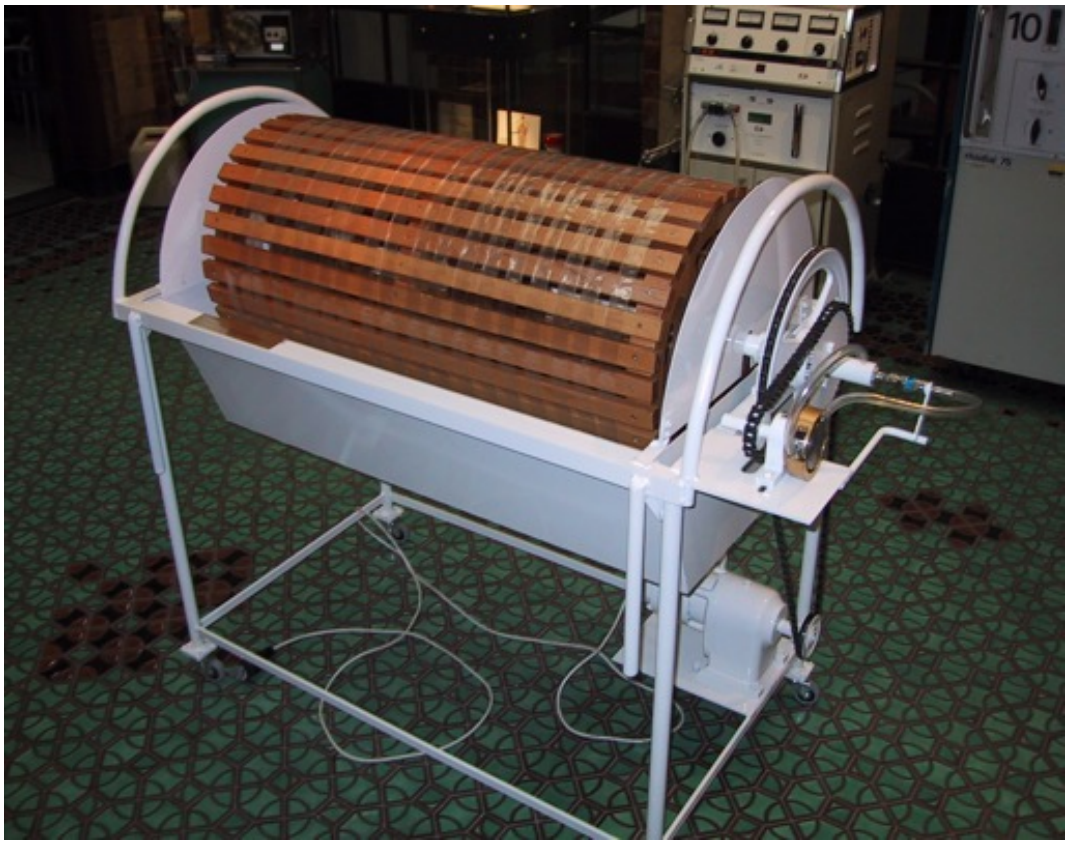


Very Expensive
€ 70000 - 90000 per year per patient

Clin Kidney J (2014) 7: 227–238

Slide provided by Prof. Joerg Vienken

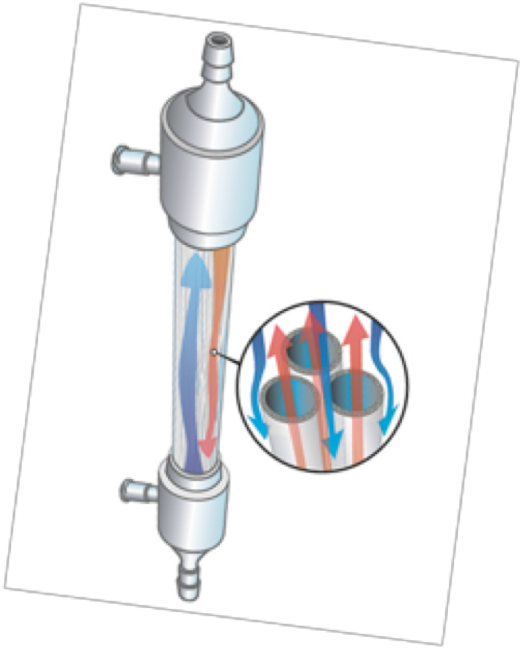
Dr. W. Kolff and
Rotating Drum
(1911 - 2009)



Sophia Schafstadt (1945)
(suffering from acute renal failure)

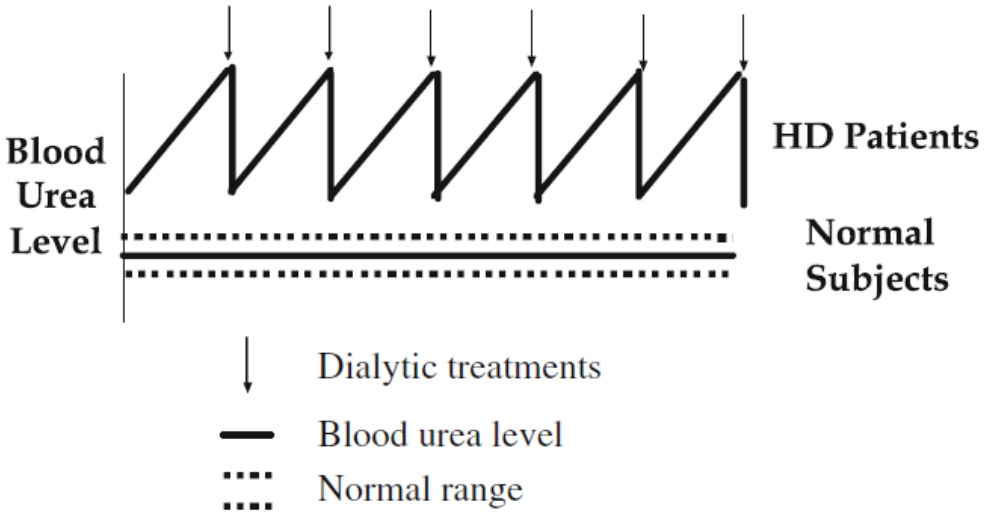
The first patient kept alive till kidney function was restored.

Current therapy



- Clearance of solutes:
  - **water soluble, low molecular weight**
  - **(some) middle molecules**
  - Not - Protein-bound solutes

- Not - continuous cleaning

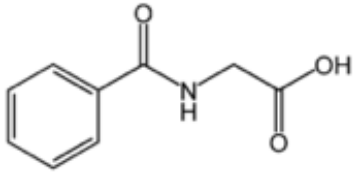


Vanholder, Kidney International 2003
Lee, Clinical and Experimental Nephrology 2008

Protein-bound solutes

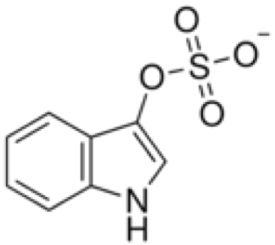
- Hippuric acid

(40% bound to HSA)



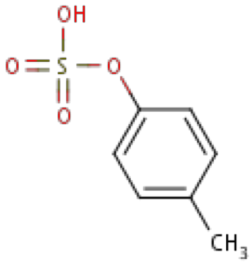
- Indoxyl sulfate

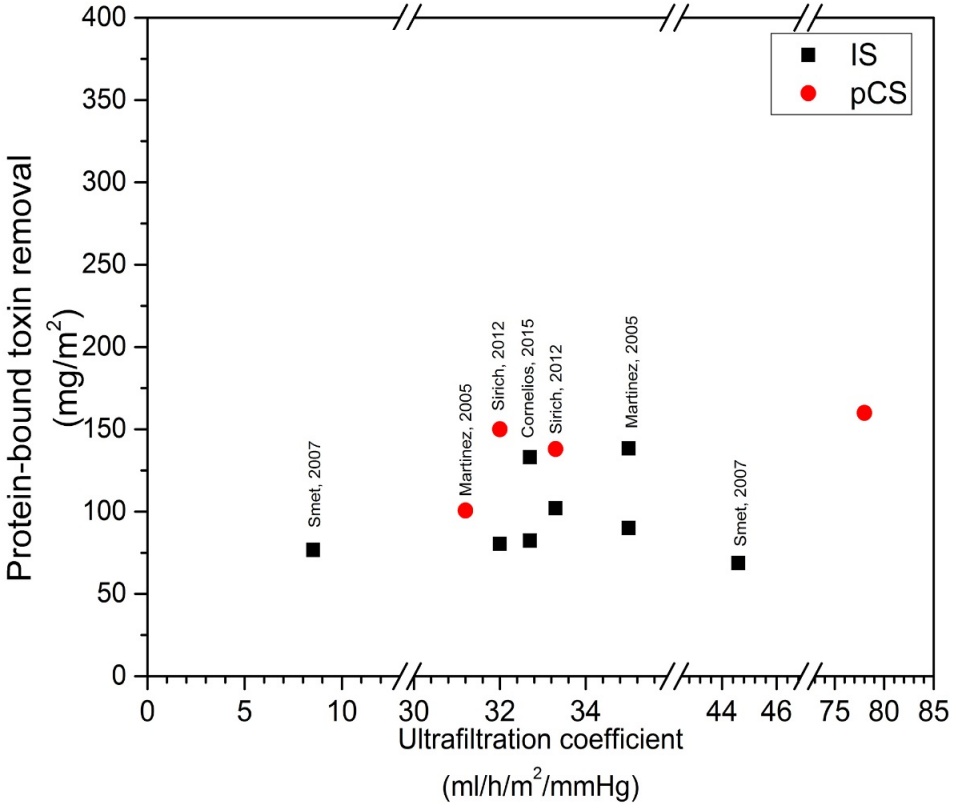
(> 90 % bound to HSA)



- P-cresyl sulfate

(> 90 % bound to HSA)

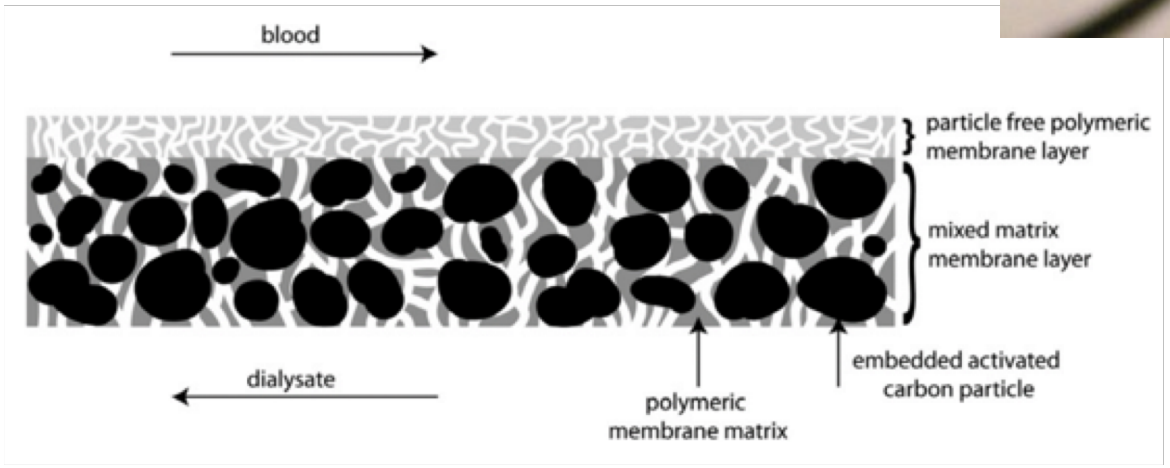




P-T ⇌ **P + T**

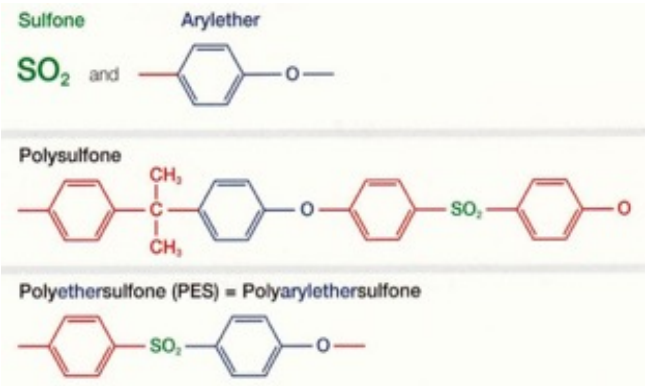
Pavlenko et al, Nature Scient. Reports (2016)

Mixed matrix membrane



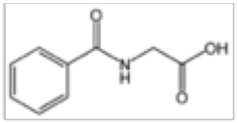
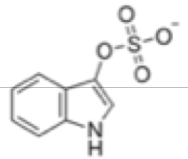
PES/PVP inner layer

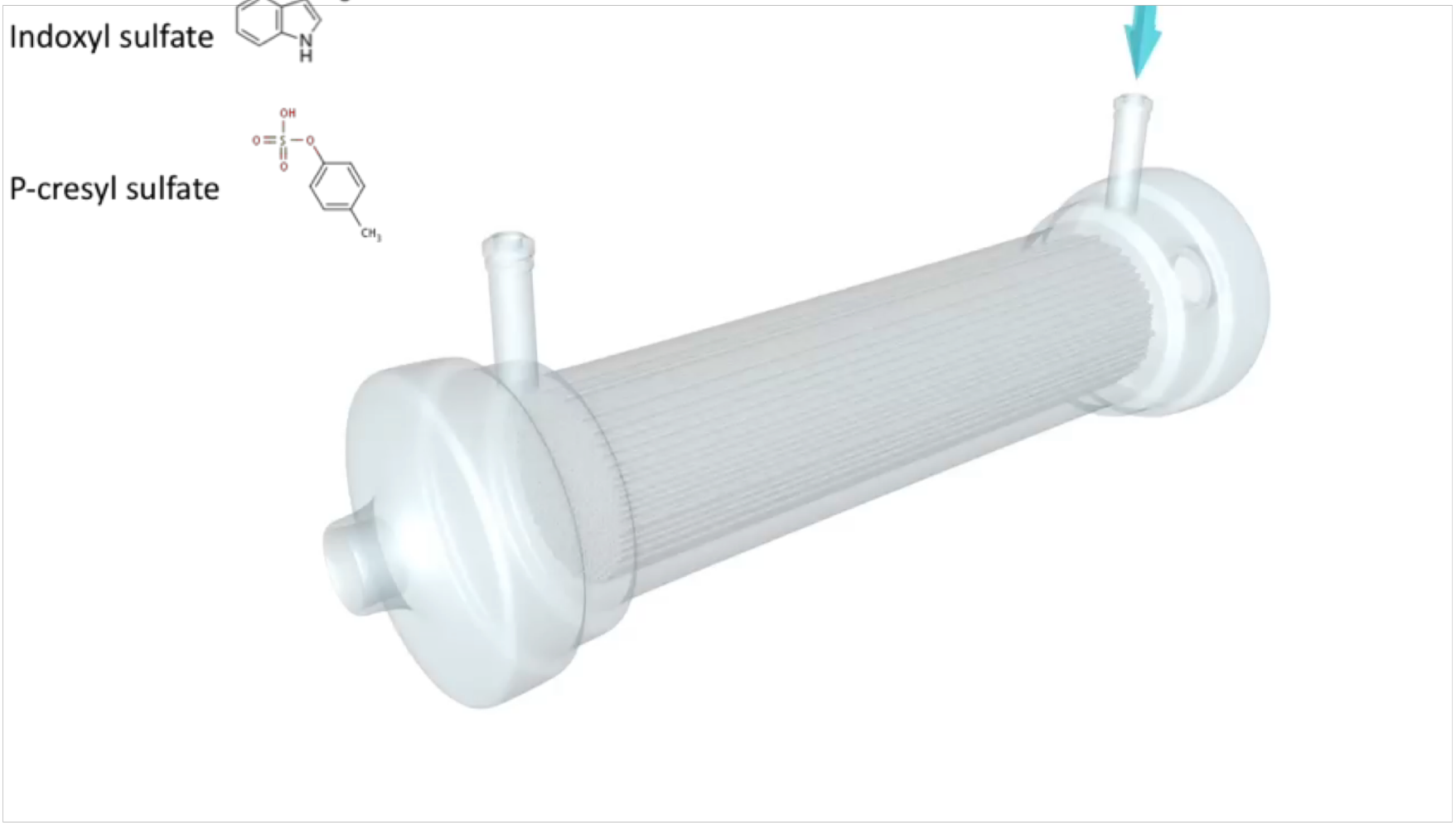
PES/PVP/AC outer layer



Biomaterials 34 (2013) p7819
Blood Purif., 37 (2014) p1
J. Mater. Chem. B, 1 (44) (2013) p6066
Acta Biomater. 8 (2012) p2279.

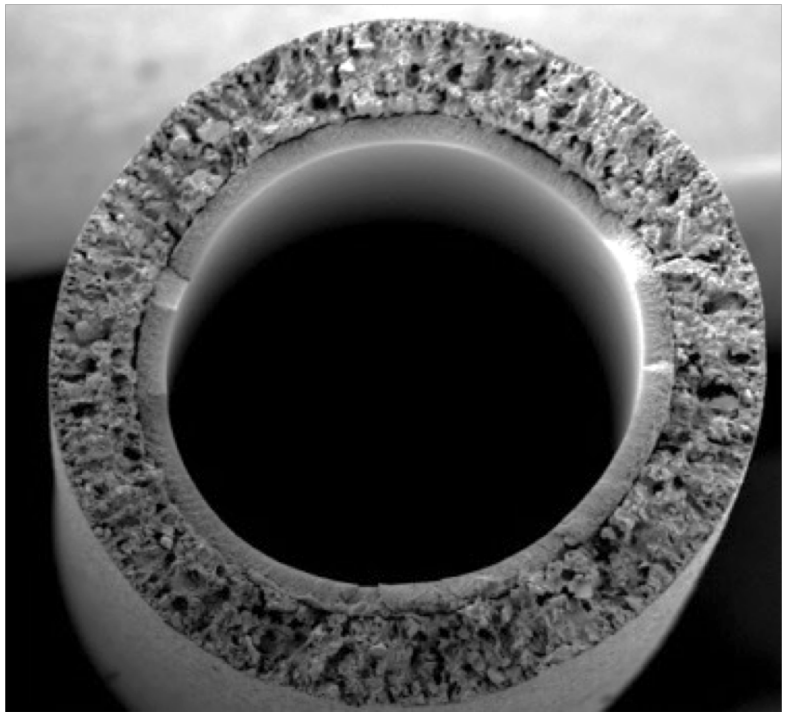
MMM concept

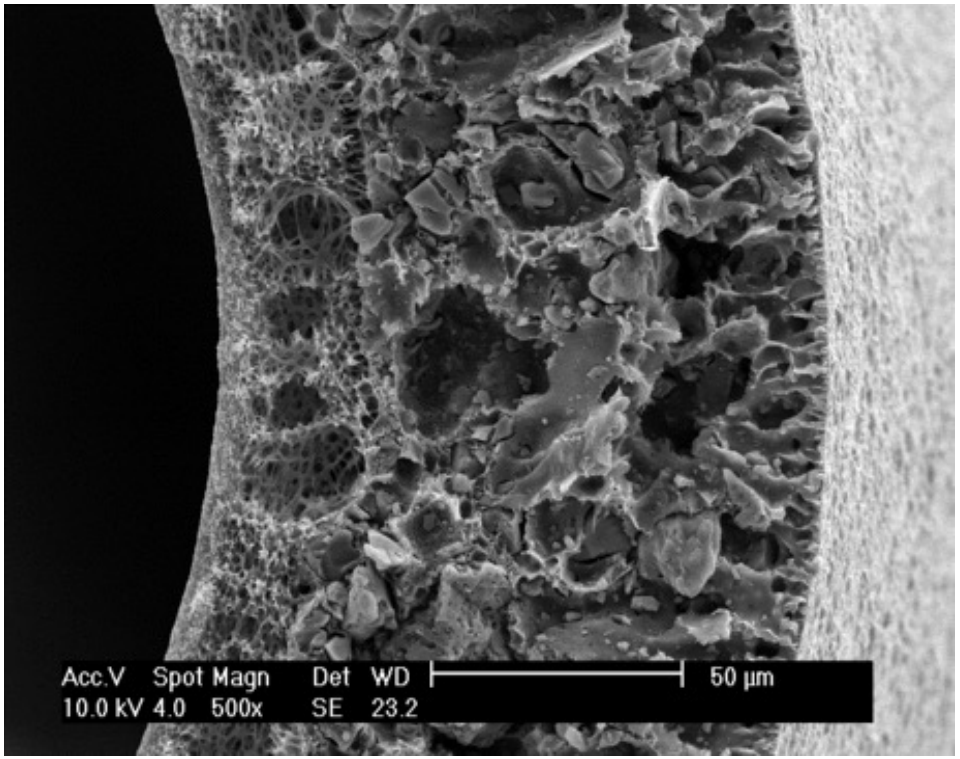
- Hippuric acid 
- Indoxyl sulfate 
- P-cresyl sulfate



P-T ⇌ **P + T**

PES/ PVP based MMM





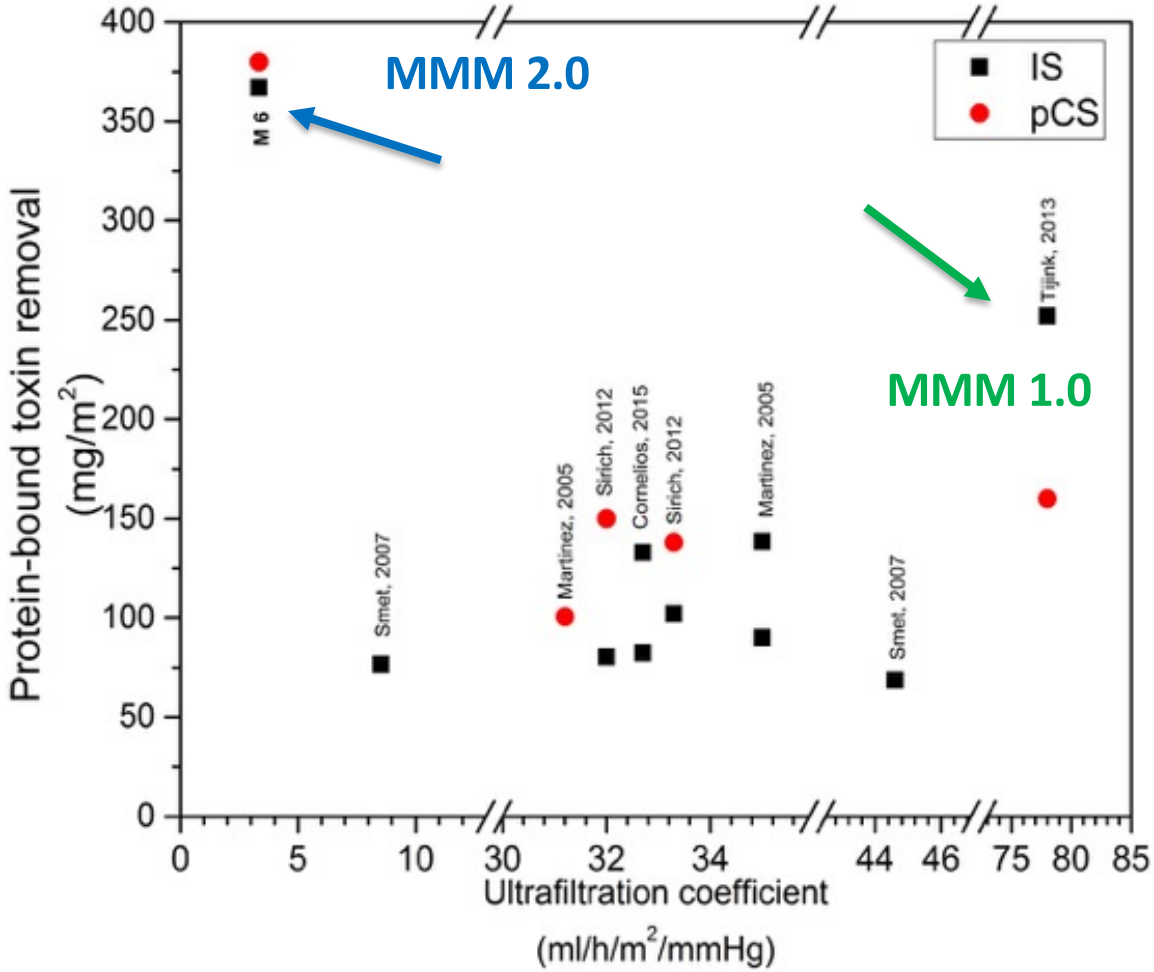
Biomaterials 34 (2013) p7819
Blood Purif., 37 (2014) p1
J. Mater. Chem. B, 1 (44) (2013) p6066
Acta Biomater. 8 (2012) p2279.

< 0.15 m^2 MMM for complete removal of PBUT

MMM 3.0 = 600 mg/m^2

UC = 75

SC albumin = 0

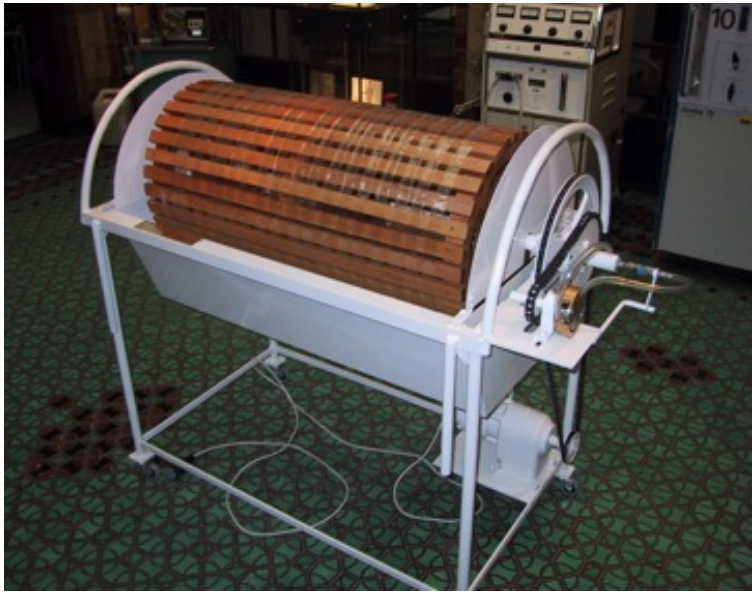


Blood compatibility

Membrane	Surface area [cm²]	WBC [%]	RBC [%]	PLT [%]	TAT [µg/L]	C5a [µg/L]	Hemolysis [%]
MMM	58	88 ± 3	100 ± 2	72 ± 10	13 ± 6	8 ± 3	0.4 ± 0.1
Polysulphone F60	250	78.± 11	101 ± 7	60 ± 9	40 ± 29	8 ± 6	0.3 ± 0.1

ISO 10993-4

eXcorLab
BIOMEDICAL RESEARCH

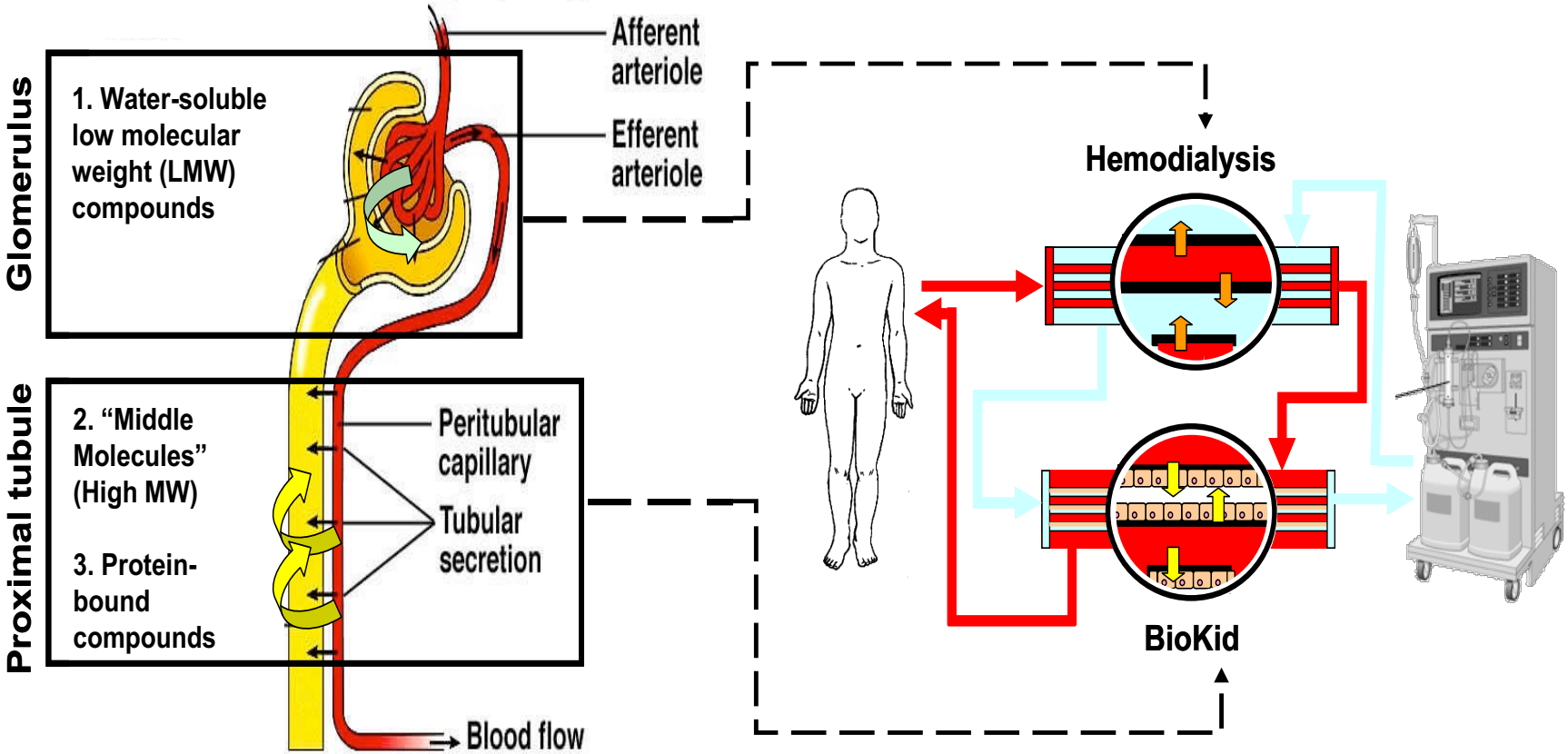


The past

The present

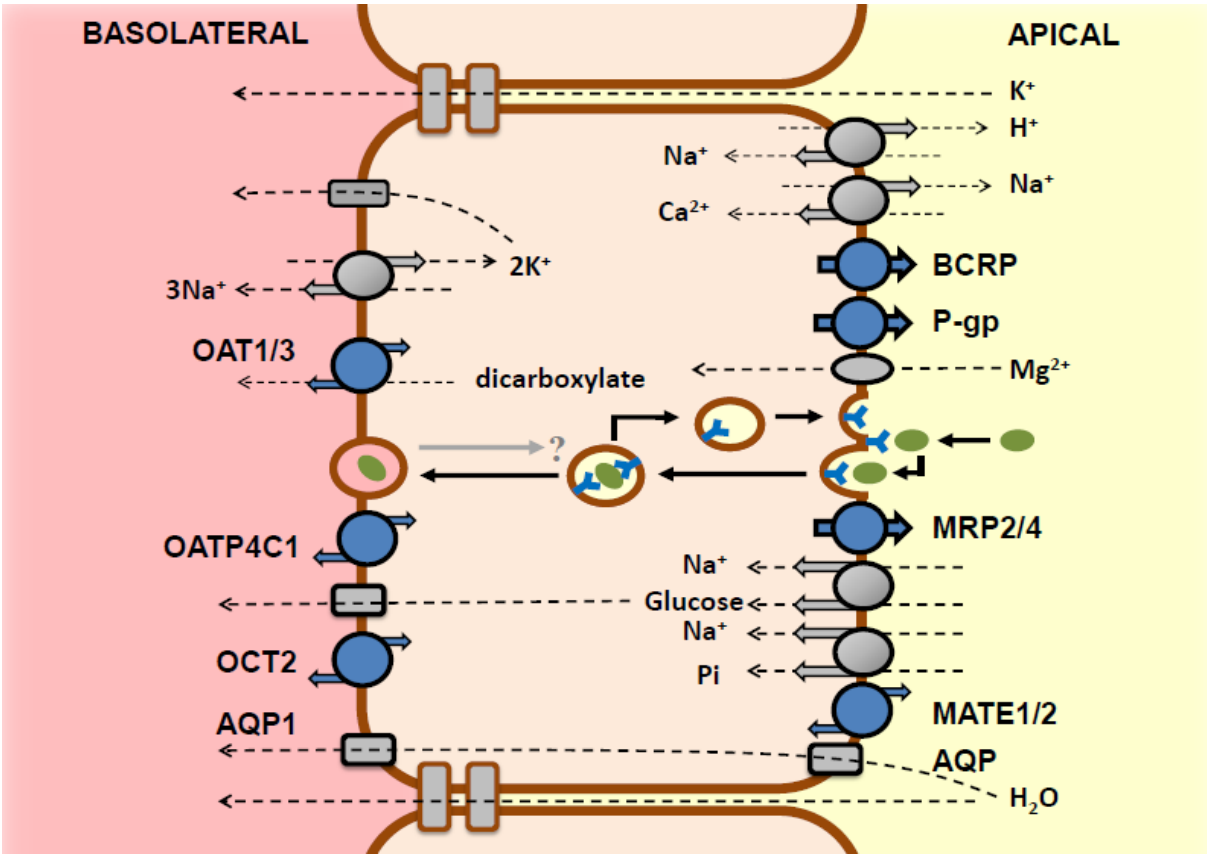
The future

Bioartificial kidney - Concept



Stamatialis et al, IJAO editorial, 2017

Transport in renal proximal tubule cells



Reabsorption mechanisms

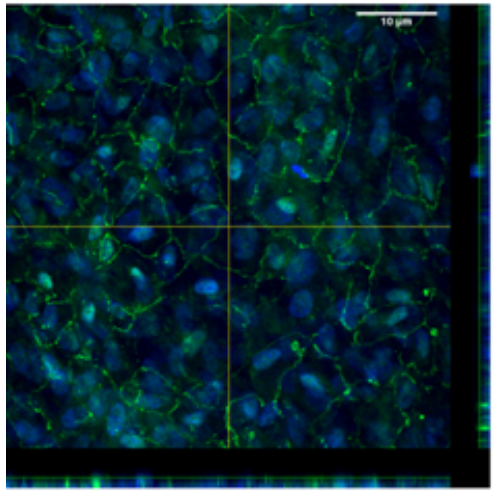
Drug transporters

Membranes for BAK, Chapt. 5,"Biomedical membranes and (bio)artificial organs", D. Stamatialis Ed, Publisher: World Scientific, 2017, ISBN: 978-981-3221-75-8

Prof. R. Masereeuw
Universiteit Utrecht
Utrecht University

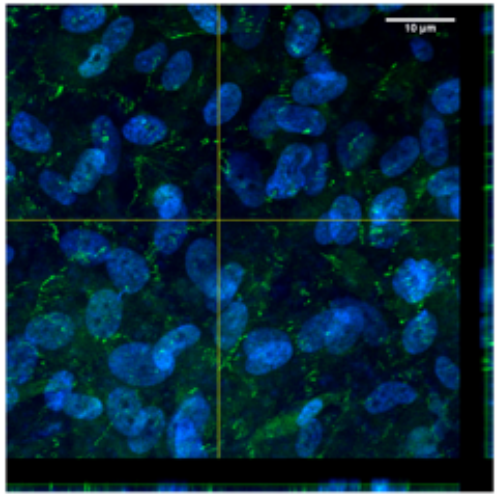
Cell origin and function

U
a **14.4**



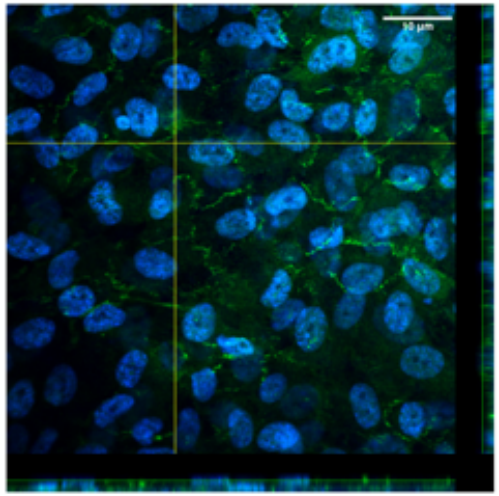
average cell size: 10.9 µm ± 0.6

T1
b **21.11**



average cell size: 19.4 µm ± 0.8***

T2
c **21.2**

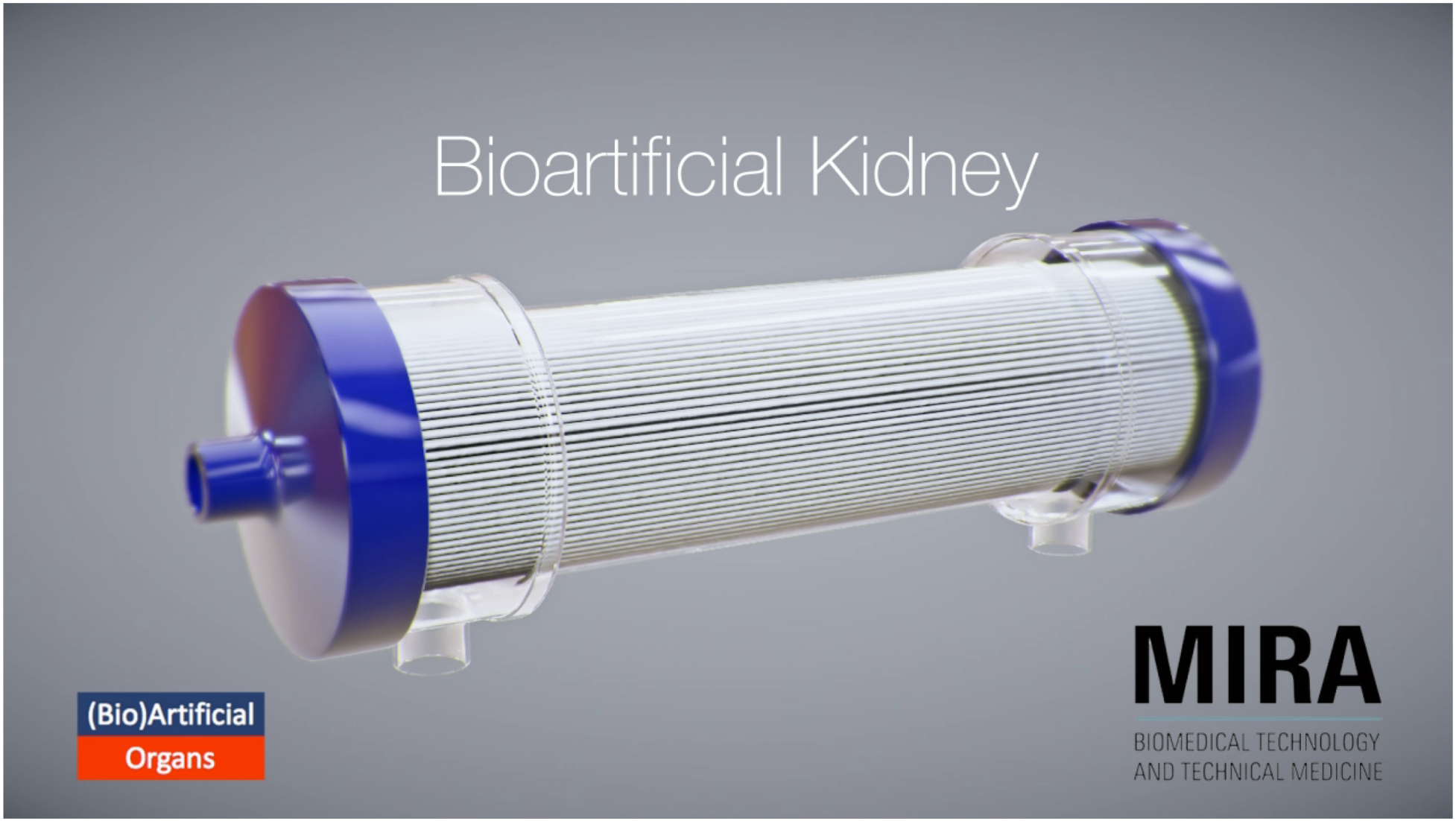


average cell size: 21.7 µm ± 0.6***

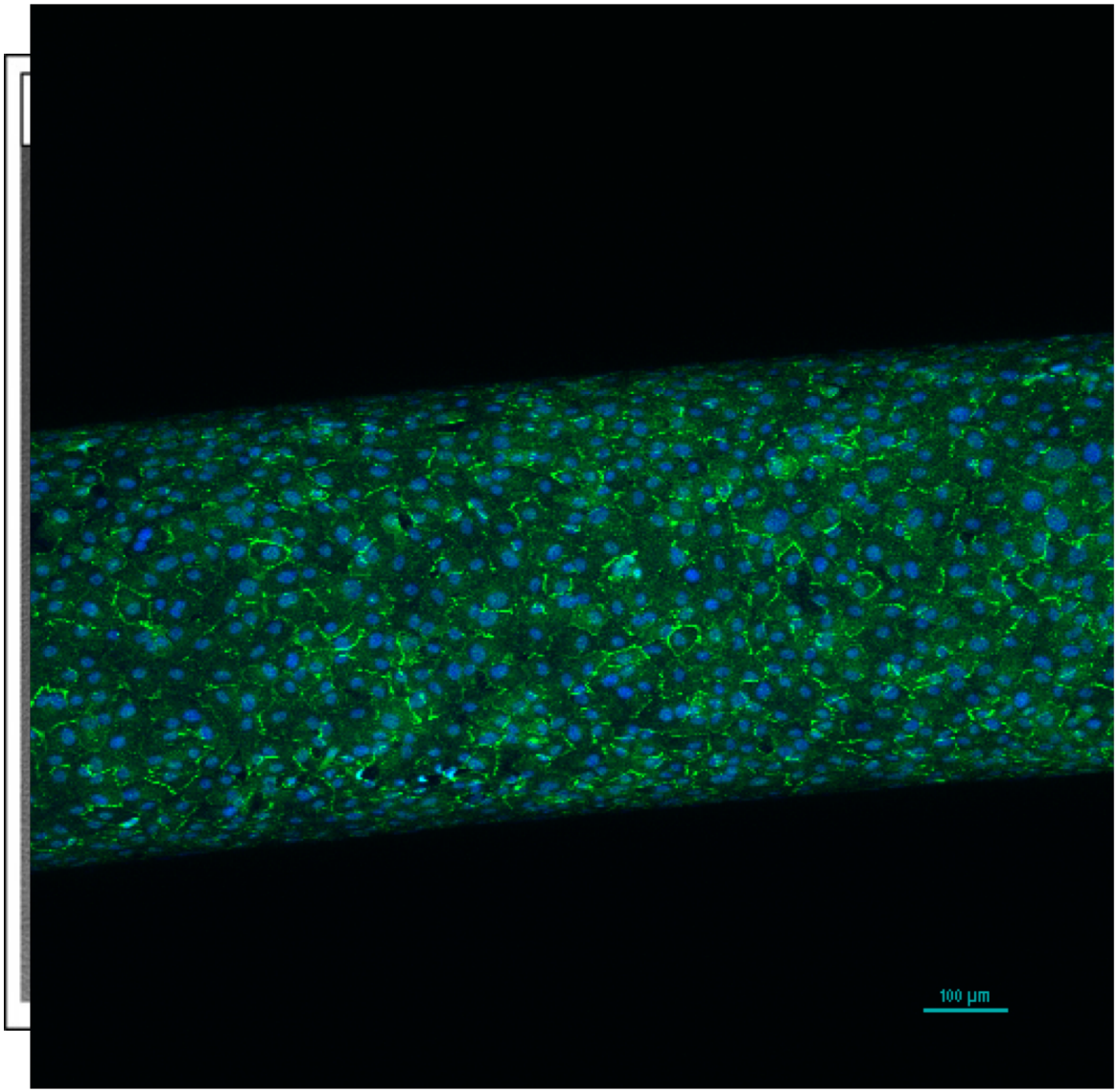
- Immortalization:
  1. SV40T tsA58 U19
  2. hTERT

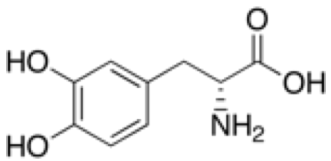
Wilmer *et al.* Cell Tissue Research 2010

Jansen, Schophuizen, *et al., Exp. Cell Res. 2014*


Bioartificial Kidney
(Bio)Artificial
Organs
MIRA
BIOMEDICAL TECHNOLOGY
AND TECHNICAL MEDICINE

“Living HFM”

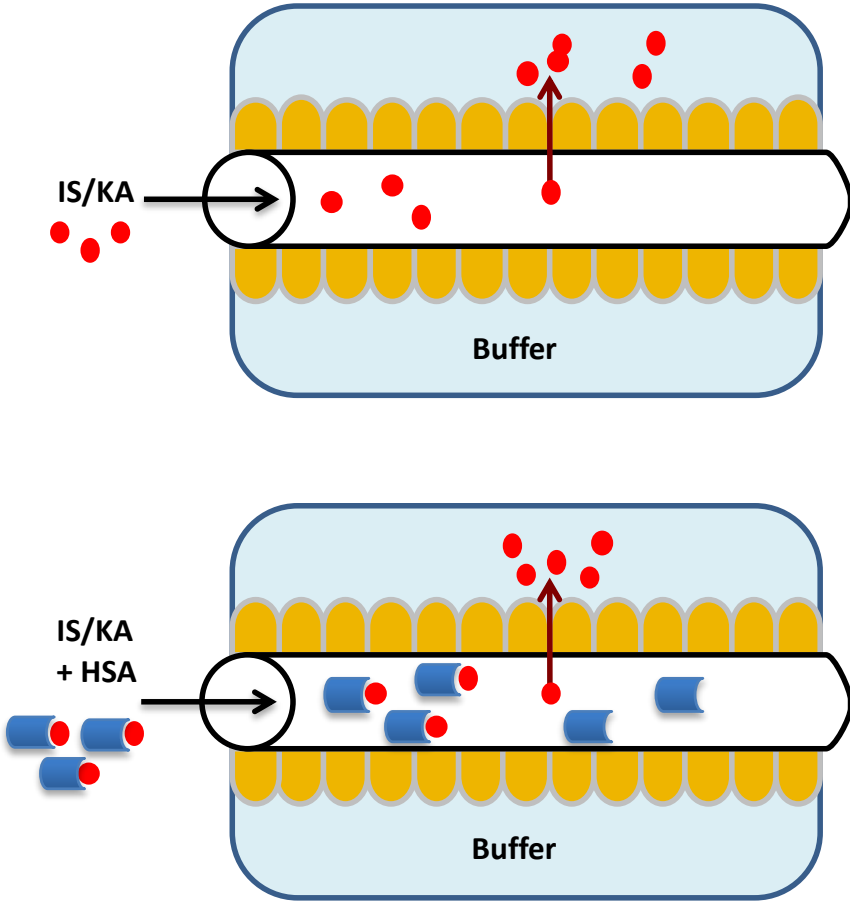


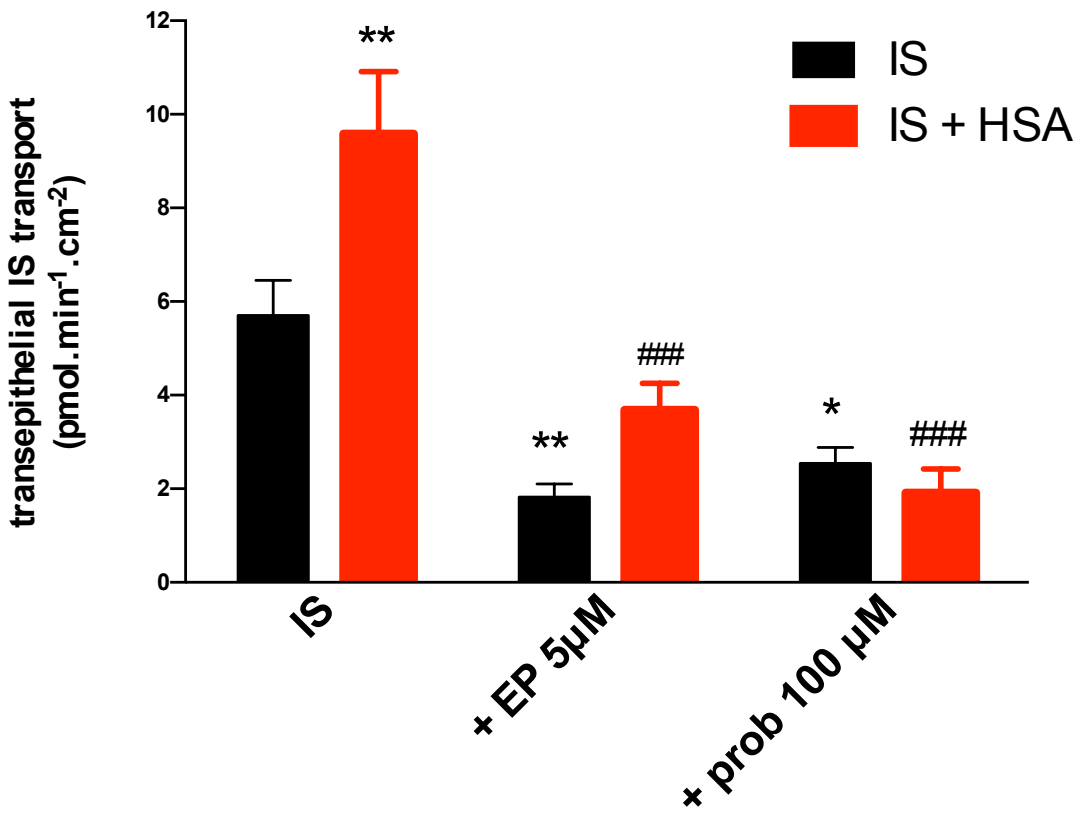


Prof. R. Masereeuw
Utrecht University

Chevtchik et al, European Journal of Pharmacology, 2016

Functional assays of PTEC on single hollow fibers
Organic anion transporters (OAT)





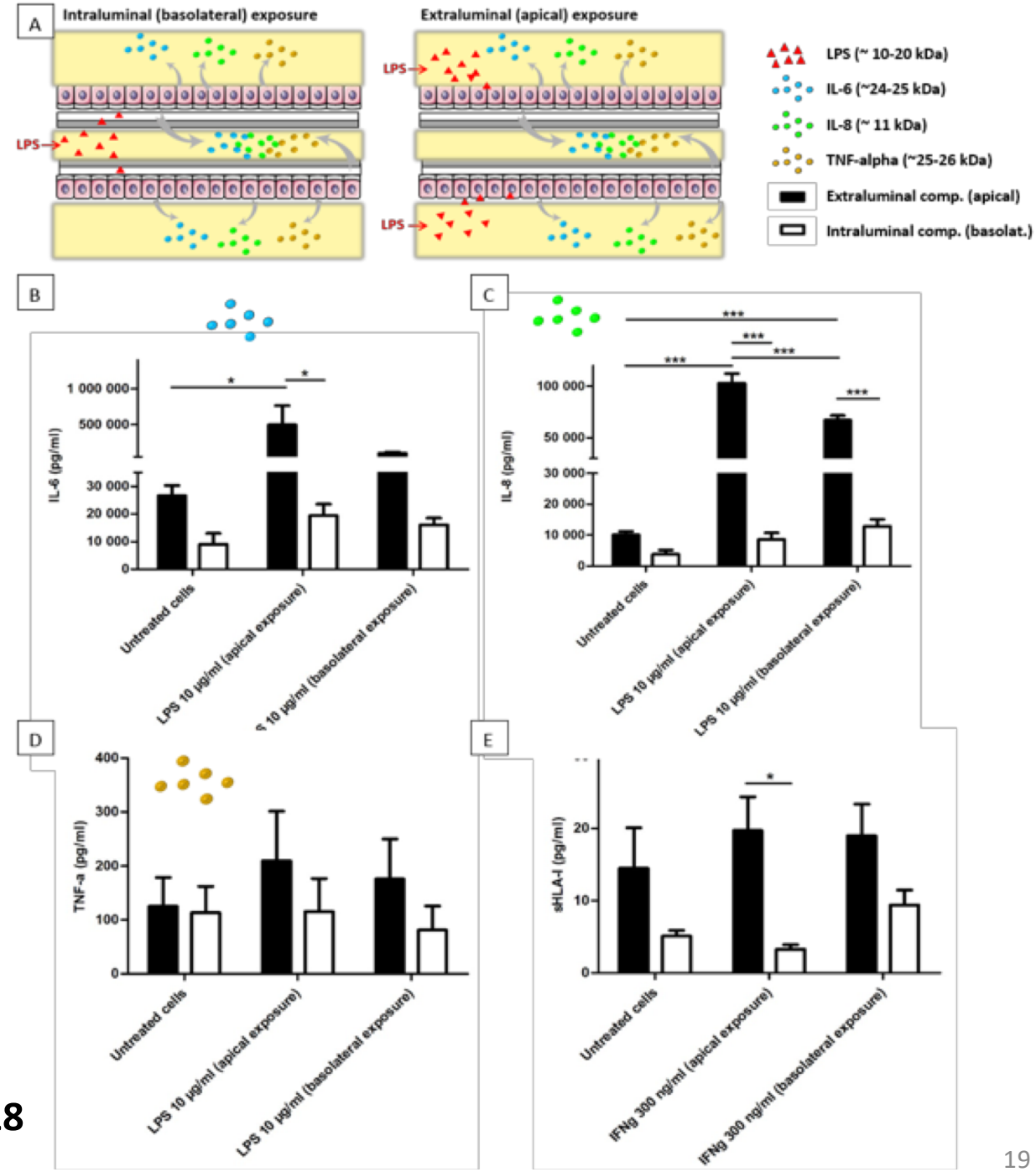
Prof. R. Masereeuw
Utrecht University

Jansen J., Fedecostante M. *et al*. Nature Sci. Rep. 2016

ciPTEC with OAT

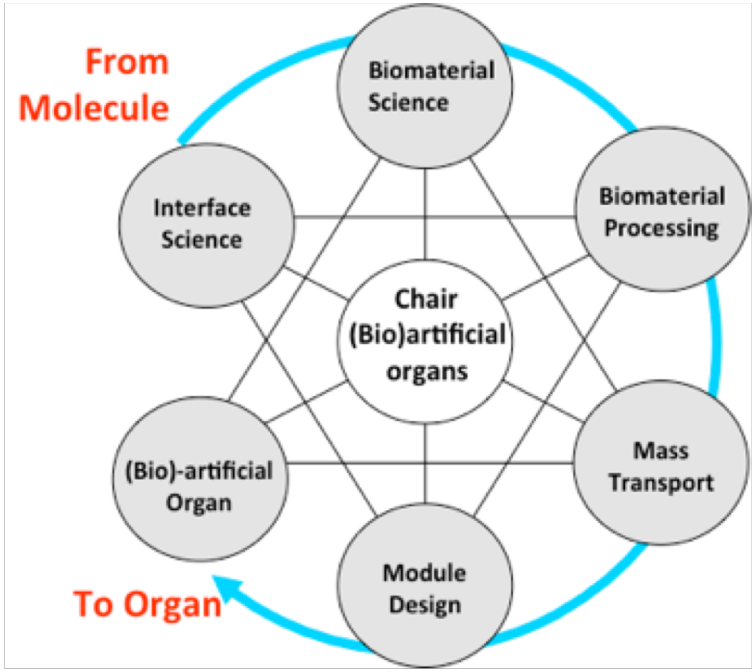
Pro-inflammatory cytokines x10 higher "Urine" compartment

Polarized secretion of immune response mediators



Chevtchic et al, JTERM, 2018

It is challenging!



Complexity increases

Artificial to Bioartificial to.. tissue engineered…

From extracorporeal to implantable…

It takes time

In vitro to *in vivo*

Acknowledgements

RadboudUMC Nijmegen
Dr. M. Wilmer

Utrecht University
M. Fedecostante
M. Mihailovic
Dr. J. Jansen
Prof. R. Masereeuw

UMC Utrecht
Dr. K. Gerritsen
Prof. M. Verhaar

Funding

BioKid BMM project

EUTox

UTwente – UMCU / UU strategic collaboration

UNIVERSITY OF TWENTE.

(Bio)Artificial
Organs